REMARKS

Applicants would like to thank the Examiner for the courtesy extended during an interview with Mr. Alexander H. Spiegler and Mr. Ken Horlick.

Applicants have cancelled claims 1 and 3 without prejudice.

Applicants have amended claims 2, 4-6 for the purpose of expediting the issuance of claims. Support for the amendment to claim 2 is found throughout the application. The specification teaches that a method for diagnosing disease is conducted on a subject (page 18, lines 19-20). The specification teaches an experimental sample is matched to one or more reference samples that match the experimental sample in at least one parameter that is determinant of physiological status, pharmacological, and/or disease status and comparing the expression profiles of the experimental and reference profiles (page 14, lines 3-6).

Support for the amendment to claims 4-6 is found throughout the application. The specification teaches that an expression profile of a common physiological state can be used as a reference sample that the best expression profile to use as a reference sample and one of the parameters of a physiological state is a reproductive state (page 15, lines 28-30; page 5, lines 21-25). The specification teaches that an experimental sample is diagnosed with the disease of the matching reference samples (page 18, lines 9-10). The specification also teaches that the women differ from men in the physiological indicator of gender, which contributes to an as yet uncharacterized level of different gene expression (page 23, lines 26-28).

It is respectfully submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested. Applicants respectfully request reconsideration of the pending rejection and reexamination of the present claims in light of the amendments and the remarks detailed below.

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which Applicants are entitled.

35 U.S.C. § 112 Rejection

The Examiner has rejected claims 1-6 under 35 U.S.C. 112, second paragraph as indefinite over the recitation of "measuring the physiological state of said experimental

sample" alleging that it is not clear as how one measures a physiological state a sample. Applicants respectfully disagree. However, for the purpose of expediting the issuance of claims, Applicants have cancelled claim 1 without prejudice. For the same reason, Applicants have amended claim 2 to delete the step of "measuring the physiology state of said experimental sample." Therefore, this rejection of claim 2 is obviated.

The Examiner has rejected claims 1-2 under 35 U.S.C. 112, second paragraph as indefinite, alleging that the recitation of "similar" which is a relative term which renders the claim indefinite. Applicants have cancelled claim 1 without prejudice. Applicants have amended claim 2 to recite "selecting reference samples of known disease state that match experimental sample in reproductive state." Therefore, this rejection of claim 2 is obviated.

The Examiner has rejected claims 1-2 under 35 U.S.C. 112, second paragraph as indefinite over the recitation of "matches," alleging that it is not clear as to what is matched between the experimental and reference samples. Applicants have cancelled claim 1 without prejudice. Applicants have amended claim 2 to recite "comparing the expression profile of said experimental sample to the expression of said reference samples to identify the reference sample that matches said experimental sample in gene expression." Therefore, this rejection of claim 2 is obviated.

The Examiner has rejected claims 3-6 under 35 U.S.C. 112, second paragraph as indefinite alleging that the claims do not recite a final process which clearly relate back to the preamble. Applicants have cancelled claim 3 without prejudice. Applicants have amended claim 4 to recite "using said profile information to diagnose physiological disorders." Applicants have amended claim 5 to recite "identifying said physiological status of said sample of unknown origin using said expression profile." Applicants have amended claim 6 to recite "using the expression profile data to identify markers of different physiological states in humans." Therefore, the rejection of claims 3-6 is obviated.

The Examiner has rejected claim 4 under 35 U.S.C. 112 as being indefinite over the recitation of "matching indicators of physiological status." Applicants have amended claim 4 to recite "comparing a gene expression profile from an experimental sample to a gene expression profile that represents an average of a plurality of reference samples with

4

matching indicators of reproductive status." Therefore, the rejection of claim 4 is obviated.

Anticipation Rejection Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 1-9 under 35 U.S.C. 102(e) as being anticipated by Friend *et. al.* (US 6,218,122). Applicants respectfully traverse this rejection.

In order to support anticipation under 35 U.S.C. 102(e), each and every element of a claimed invention must be disclosed within a single prior art reference.

Applicants have amended claims 2, 4-6 by deleting "physiological" and inserting "reproductive" in the same place. Applicants respectfully submit that Friend *et. al.* does not disclose comparing gene expression of samples with matching reproductive state. Therefore, the rejection under 102(e) should be withdrawn.

The Examiner has rejected claim 3 under 35 U.S.C. 102(e) as being anticipated by Lockhart *et. al.* (US 6,033,860). However, Applicants have cancelled claim 3 without prejudice. Therefore, this rejection is obviated.

CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5699.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,

Wei Zhou
Reg. No.: 44,419

Date: 7/11/2002

Legal Department
Affymetrix, Inc.
3380 Central Expressway
Santa Clara, CA 95051
Tel: 408/731-5000
Fax: 408/731-5392

In the Claims

Please amend Claim 2, 4-6 as follows:

2. (amended) A method for diagnosing disease <u>in a subject using</u> [in] an experimental sample <u>derived from said subject</u> comprising:

   [measuring the physiological <u>reproductive</u> state of said experimental sample;]

   selecting reference samples of known disease state that is [similar] <u>matched</u> to said experimental sample in [physiological] <u>reproductive state</u>; and

   comparing the expression profile of said experimental sample to the expression of said reference samples to identify the reference sample that matches said experimental sample <u>in gene expression</u>; and

   diagnosing the experimental sample with the disease of the matching reference sample.

4. (amended) A method to diagnose physiological disorders comprising:

   comparing a gene expression profile from an experimental sample to a gene expression profile that represents an average of a plurality of reference samples with matching indicators of [physiological] <u>reproductive</u> status; <u>and</u>

   <u>using said profile information to diagnose physiological disorders.</u>

5. (amended) A method to identify the [physiological] <u>reproductive</u> status of a sample [of unknown origin] comprising:

   generating an expression profile from the experimental sample, and

   comparing said expression profile to a plurality of expression profiles of known [physiological] <u>reproductive</u> state[.]<u>; and</u>

   <u>identifying said physiological status of said sample of unknown origin using said expression profile.</u>

6. (amended) A method to identify markers of different [physiological] <u>reproductive</u> states in [humans] <u>women</u> comprising:

6

matching a sample from a first physiological state from a second physiological state;

comparing the expression profiles from said first and second physiological states; and

identifying genes that are differentially expressed in said first and second [physiological] reproductive states[.] ; and

using the expression profile data to identify markers of different physiological states in humans.